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EXAMINER	
GANGLE, BRIAN J	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,055	MATTSBY-BALTZER ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-25,27,28 and 34-36* is/are pending in the application.

4a) Of the above claim(s) *21-23,27,29 and 34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-25 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and remarks, filed 4/11/2007, are acknowledged. Claims 24, 25, and 28 are amended. Claims 1-20, 26, 30-33, and 37-39 are cancelled. Claims 21-25, 27-28, and 34-36 are pending. Claims 21-23, 27, 29, and 34-36 are withdrawn as being drawn to non-elected inventions. Claims 24-25 and 28 are currently under examination.

Specification

The objection to the specification for the use of the trademarks is maintained for the reasons set forth in the previous office action. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Applicant's amendment to page 7 of the specification is noted. However, applicant should review the specification to correct any other use of trademarks. TWEEN and EXTRAVIDIN are both trademarks that can be found on page 8. Further, generic terminology describing the trademarked material must accompany trademarks. It is suggested that applicant refer to manufacturer information to find this terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

It should be noted that the cited occurrence of improper use is only exemplary and applicant should review the specification to correct any other use of trademarks.

Claim Objections Withdrawn

The objections to claims 24-26, 28, 30-33, and 37-39, because claims 24-26, 28, 30-33, and 37-39 are dependent on non-elected claims; claims 31 and 32 are substantially duplicates; and claims 38 and 39 are substantially duplicates, is withdrawn in light of applicant's amendment thereto.

Claim Rejections Withdrawn

The rejection of claims 31-32 and 38-39 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, is withdrawn. The cancellation of these claims renders the rejection moot.

The rejection of claims 24-26, 28, 30-33, and 37-39 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, is withdrawn in light of applicant's amendment to claims 24-25 and 28, and the cancellation of claims 26, 30-33, and 37-39.

The rejection of claim 26 as being rendered vague and indefinite by the phrase "wherein said diagnosis is performed on mucosal secretions or urine," is withdrawn. The cancellation of this claim renders the rejection moot.

The rejection of claim 28 for lacking antecedent basis for the limitation "said patient" in line 4, is withdrawn in light of applicant's amendment thereto.

The rejection of claim 33 as being rendered vague and indefinite by the phrase "wherein said diagnosis is performed on mucosal secretions or urine," is withdrawn. The cancellation of this claim renders the rejection moot.

The rejection of claims 37-39 for insufficient antecedent basis is withdrawn. The cancellation of these claims renders the rejection moot.

The rejection of claims 24-26, 30, and 33 under 35 U.S.C. 102(b), as being anticipated by Brawner *et al.* (J. Clin. Microbiol., 27:1335-1341, 1989), is withdrawn in light of applicant's amendment thereto.

The rejection of claims 24-26, 30, and 33 under 35 U.S.C. 102(b), as being anticipated by Bargatze *et al.* (PCT Publication WO 00/48633, 8/2000), is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 24-25, and 28under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained for the reasons set forth in the previous office action.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues: that "the amended claims correspond to the disclosed method with respect to species disclosed of antigen and antibody, and particularly corresponds to the examples given by applicant in the specification." Applicant also argues that the term associated no longer appears in the claims.

Applicant's arguments have been fully considered and deemed non-persuasive.

While applicant has removed the term "associated" from the claims, thereby limiting the method to antibodies that are reactive with β(1-3)- and/or a β(1-3) (1-6)-glucans, applicant still has not fully characterized the antigen or the antibodies needed to perform the method. As stated previously, using antibodies that bind to an epitope found on β(1,3)- and/or β(1,3)(1,6)-glucans, one would be unable to differentiate between plant species and particular fungal species because these polysaccharides are found in numerous plants and species of fungi, thus. The specification is silent regarding what epitopes would allow one to differentiate between species. Therefore, the specification does not describe, with any degree of specificity, the β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes to which the members of the claimed genus of antibodies must bind in order to achieve the desired immunological response, such that the specification might reasonably convey to the skilled artisan that applicant had possession of the claimed invention at

the time the application was filed. Nor has applicant described, with any degree of specificity, the claimed antibodies themselves.

As outlined previously, the instant claims are drawn to methods of diagnosis of a fungal infection comprising assaying with at least one antibody that is monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan epitope in free form, in cell wall fragments or on an intact cell surface and available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans*.

The courts have recently decided in Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin (CAFC, 02-1187, 1/20/2004) that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR

antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

In the instant application, applicant has failed to "fully characterize" the antigen (i.e. β(1,3)- and/or β(1,3)(1,6)-glucan epitopes) to which the claimed antibody binds. The instant claims are drawn to all monoclonal antibodies with specificity to any β(1,3)- and/or β(1,3)(1,6)-glucan epitope. If one were to limit the epitope to β(1,3)- and/or β(1,3)(1,6)-glucans, these polysaccharides are found in numerous plants and species of fungi, thus one would be unable to differentiate between plant species and particular fungal species. The specification is silent regarding what epitopes would allow one to differentiate between species.

The specification refers to the antibody "A10A," which refers to a laboratory designation for a monoclonal antibody. Said designation does not provide any structural or functional limitations. Moreover, there is no description in the application of the structure of said antibody. Consequently, since applicant has not fully characterized the antigen to which the claimed antibodies bind, the written description requirements under 35 U.S.C 112, first paragraph have not been met.

The specification does not describe, with any degree of specificity, the β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes to which the members of the claimed genus of antibodies must bind in order to achieve the desired immunological response, such that the specification might reasonably convey to the skilled artisan that applicant had possession of the claimed invention at the time the application was filed. Nor has applicant described, with any degree of specificity, the claimed antibodies themselves.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable

from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by applicant in the specification; nor has applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has applicant described distinguishing identifying characteristics sufficient to show that applicant were in possession of the claimed invention at the time the application was filed.

As evidenced by Greenspan et al. (Nature Biotechnology 17: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an

antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes to which the members of the claimed genus of antibodies must bind, which are critical or essential to the binding, one skilled in the art would not recognize that applicant had possession of the claimed invention at the time the application was filed.

The rejection of claims 24-25, and 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained for the reasons set forth in the previous office action.

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Applicant argues: that "the amended claims correspond to the disclosed method with respect to species disclosed of antigen and antibody, and particularly corresponds to the examples given by applicant in the specification." Applicant also argues that the term associated no longer appears in the claims.

Applicant's arguments have been fully considered and deemed non-persuasive.

While applicant has removed the term "associated" from the claims, thereby limiting the method to antibodies that are reactive with β(1-3)- and/or a β(1-3) (1-6)-glucans, applicant still has not fully characterized the antigen or the antibodies needed to perform the method. The specification fails to describe immunoepitopes against which the claimed antibodies are raised and must subsequently bind. The working examples disclose specific antibodies that meet the limitations of the instant claims. However, these "examples" refer to antibodies by their laboratory designations which are not sufficient to provide enablement for the full scope of the rejected claims. The specification is silent as to what specific "immunoepitope" meets the

limitations of the claims. Additionally, the specification is silent with regard to what epitopes are cross-reactive and what epitopes would allow one to differentiate between species. There is no showing in the specification that either A10A, or any other antibodies can be used to detect infection using any type of sample.

As outlined previously, undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the claimed invention without undue experimentation.

Nature of the invention: The instant claims are drawn to methods for the diagnosis of a fungal infection comprising assaying with at least one antibody wherein said antibody is a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan epitope in free form, in cell wall fragments or on an intact cell surface; wherein said glucan associated epitope is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans.*

Breadth of the claims: The instant claims are drawn to all antibodies with specificity to any β(1,3)- and/or β(1,3)(1,6)-glucan epitope (claims 24-25). Claim 28 is drawn to all monoclonal antibodies with specificity to any β(1,3)- and/or β(1,3)(1,6)-glucan epitope. With the exception of claim 25, the claims are drawn to methods of diagnosing all fungal infections of all types. This would include every species of fungus capable of causing infection, and it would include mycoses of all types, including systemic, epidermal, nail, and gastrointestinal infections. The claims encompass antibodies directed to β(1-3)- and/or a β(1-3) (1-6)-glucan epitopes from all organisms.

Working Examples/Guidance of Specification: The specification fails to describe immunoepitopes against which the claimed antibodies are raised and must subsequently bind. The working examples disclose specific antibodies that meet the limitations of the instant claims. However, these "examples" refer to antibodies by their laboratory designations which are not sufficient to provide enablement for the full scope of the rejected claims. The specification is silent as to what specific "immunoepitope" meets the limitations of the claims. Additionally, the

specification is silent with regard to what epitopes are cross-reactive and what epitopes would allow one to differentiate between species. There is no showing in the specification that either A10A, or any other antibodies can be used to detect infection using any type of sample. The only information regarding A10A or other antibodies is that they are capable of binding β(1-3)- and/or a β(1-3) (1-6)-glucans. The specification states that β(1,3)-glucan has been found in the serum of all patients with candidemia, but in none of women with superficial Candida infection, or in healthy controls (page 14). The specification further states that "the presence of β(1,3)-glucans in the serum of patients with deep fungal infections may be a useful marker for laboratory diagnosis of these infections. Future investigations will address the usefulness of our mAbs to glucan in an immunoassay-based kit for the rapid detection of β(1,3)-glucans in blood samples, in other specimens from patients with invasive fungal infections, or in other body fluids such as mucosal secretions and urine." All guidance regarding the claimed method is prophetic.

State of the prior art and Unpredictability of the art: In the instant application, applicant has failed to "fully characterize" the antigen (i.e. β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes) to which the claimed antibody binds. The instant claims are drawn to methods utilizing all antibodies with specificity to any β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes. Consequently, since applicant has not fully characterized the antigen to which the claimed antibodies bind, hence the skilled artisan would not be able to make the claimed invention.

While the skill in the art of immunology is high, to date, prediction of a specific immune response for any given composition in any given animal is quite unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid

substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally, Greenspan et al. (Nature Biotechnology 17: 936-937, 1999), disclose defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a particular immune response (i.e. generation of an antibody that bind to a given epitope) can only be identified empirically. This constitutes undue experimentation. Therefore, given the lack of success in the art, the lack of working examples commensurate in scope to the claimed invention and the unpredictability of the generation of a specific immune response, the specification does not enable any person of skill in the art to which it pertains, or with which it is most nearly connected, to make and use the claimed invention.

With regard to methods of diagnosing fungal infections, monoclonal antibodies capable of binding to β(1,3)-glucans have been shown in the art, and assays exist for determining the presence of β(1,3)-glucans in environmental samples, as well as serum samples. Tamura et al. (J. Clin. Lab. Anal., 11:104-109, 1997) disclose an assay to detect Candida β(1,3)-glucans in murine serum samples (see Results). Milton et al. (Appl. Environ. Microbiol., 67:5420-5424, 2001) present an ELISA to determine the presence of β(1,3)-glucans in environmental samples (see whole article). However, these studies have shown an ability to detect β(1,3)-glucans, not to diagnose infection, or to determine the presence of fungal cells, especially in specific areas of the body. Tamura only studied serum samples, and in these did not show a statistically valid correlation between fungal cells and β(1,3)-glucans. Using methods other than antibody detection, Odabasi et al. (Clin. Infect. Dis., 39:199-205, 2004) found serum samples that were positive for β(1,3)-glucans in patients with no known fungal infections, and found serum samples

that were negative for β(1,3)-glucans in patients that likely had fungal infections (see page 204, column 1, paragraph 3 – column 2, paragraph 2; see also, table 2). Murray et al. (Medical Microbiology, 4th ed., 2002) state that Candida species can be isolated from healthy mucosal surfaces of the oral cavity, vagina, gastrointestinal tract, and rectal area. As many as 80% of people may show colonization of these sites in the absence of disease (see page 664, column 2, paragraph 3).

Therefore, while monoclonal antibodies may be used to detect the presence and the amount of β(1,3)-glucans present in a sample, this is not correlated with infection. Applicants have not shown the method to be effective, and only prophetically discuss said method. Applicants stated that in patients with superficial infection, no β(1,3)-glucans were found in serum. This is in agreement with the art that shows that β(1,3)-glucans were not detected in some infected patients. The skilled artisan would expect that urine samples would not be predictive of dermatophytic infections, and that oral samples would not be predictive of vaginal infections. Further, one would be unable to distinguish between Candida vaginitis or mucocutane candidiasis and the normal colonization that is found in 80% of the population using said method. Moreover, the epitopes to which the claimed antibodies must bind are present in many species. One would be unable to distinguish between these species using the claimed methods, and since said epitopes can be found on plant cells, one could not even determine if the β(1,3)-glucans were fungal in origin.

Therefore, in view of the lack of guidance in the specification and the art, the specification does not enable one of skill in the art to use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained for the reasons set forth in the previous office action.

Applicant argues: that the claim is now clear due to the amendment of the claim, adding the limitation "caused by."

Applicant's arguments have been fully considered and deemed non-persuasive.

The phrase "caused by" does not render the claim definite. Candida vaginitis is a disease caused by a fungal infection, it is not the infection itself. In addition, mucocutane candidiasis is a heterogeneous disorder of the immune system that is characterized by persistent Candida infections of the mucous membranes. As with Candida vaginitis, mucocutane candidiasis is a disease caused by a fungal infection, and it is not the fungal infection itself. Therefore, a fungal infection cannot be "caused by" the disease that it causes.

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 24 and 28 are rejected under 35 U.S.C. 102(b), as being anticipated by Wakshull *et al.* (PCT Publication WO 99/31510, 6/1999), is maintained for the reasons set forth in the previous office action.

Applicant argues: that Wakshull discloses methods of isolating β(1-3)- or a β(1-3) (1-6)-glucan containing organisms in a sample, utilizing various binding agents that are not antibodies. Applicant asserts that, although Wakshull "mentioned that antibodies can be used," they do not teach or suggest assaying mucosal secretions or urine, nor do they teach diagnosis of a fungal infection in a patient.

Applicant's arguments have been fully considered and deemed non-persuasive.

Contrary to applicant's assertion, Wakshull discloses each of the limitations of the rejected claims. In the paragraph bridging pages 18 and 19, Wakshull states, "detection and quantitation of the presence of β(1-3)-glucan, or of β(1-3)-glucan containing organisms, is useful in the diagnosis of fungemias or fungal contamination. To diagnose fungal infection in an

individual, for example, a sample, such as a biological fluid sample, is obtained from the individual. The sample is assayed for the presence of β(1-3)-." In lines 19-25 of page 19, Wakshull go on to state that antibodies to β(1-3)-glucan are useful in the methods and assays described. This is quite clearly a disclosure of an assay using antibodies in a method of diagnosing fungal infection. Also, as previously stated, Figures 7 and 8 show that the biological sample can be urine.

As outlined previously, the instant claims are drawn to a method for the diagnosis of a fungal infection comprising assaying mucosal secretions or urine of a patient with at least one antibody wherein the antibody is a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan epitope in free form, in cell wall fragments or on an intact cell surface and available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claim 24). Claims are also drawn to a method for diagnosing fungal infections comprising performing an assay for the detection of β(1,3)-glucans in a sample using a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitope in free form, in cell wall fragments or on an intact cell surface, and wherein the presence of β(1,3)-glucans indicates a fungal infection in said patient and wherein the where the β(1-3)- and/or β(1-3) (1-6)-glucan associated epitope is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claim 28).

Wakshull *et al.* disclose a method of diagnosis of fungal infection where a sample is obtained from an individual and said sample is assayed, with monoclonal antibodies for the presence of β(1,3)-glucans, which would be indicative of infection (see page 19, lines 1-10 and 19-25). The biological sample can be human urine, and said antibodies can bind to β(1,3)-glucans from *Candida albicans* (see figures 7-8).

New Claim Rejections

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-25 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24 and 28 are rendered vague and indefinite by the phrase, "reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan epitope in free form, in cell wall fragments or on an intact cell surface and available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans*." Based on the sentence structure and use of commas, it is not clear what form the epitopes are in. Are both the β(1-3)- and β(1-3) (1-6)-glucan epitopes to be "in free form, in cell wall fragments or on an intact cell surface and available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans*", or is it just the β(1-3) (1-6)-glucan epitopes that are to be available in these forms? Also, what is to be available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans*?

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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